



AM100788

SEQUENCE LISTING

<110> WYETH HOLDING CORPORATION.; KUNZ, ARTHUR ET AL.

<120> CALICHEAMICIN DERIVATIVE-CARRIER CONJUGATES

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<213> mouse

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<223> 5/44g CDR-H1

<220>

<221>

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Asn Tyr Trp Ile His

1 5

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Gly Ile Asn Pro Gly Asn Asn Tyr Thr Thr Tyr Lys Arg Asn Leu Lys

1 5 10 15

Gly

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<210> 6  
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&lt;220&gt;

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&lt;220&gt;

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&lt;400&gt; 7

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 1 5 10 15

Asp Gln Val Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Ala Asn Ser  
 20 25 30

Tyr Gly Asn Thr Phe Leu Ser Trp Tyr Leu His Lys Pro Gly Gln Ser  
 35 40 45

Pro Gln Leu Leu Ile Tyr Gly Ile Ser Asn Arg Phe Ser Gly Val Pro  
 50 55 60

Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile  
 65 70 75 80

Ser Thr Ile Lys Pro Glu Asp Leu Gly Met Tyr Tyr Cys Leu Gln Gly  
 85 90 95

Thr His Gln Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys  
 100 105 110

Arg

&lt;210&gt; 8

&lt;211&gt; 121

&lt;212&gt; PRT

&lt;213&gt; mouse monoclonal 5/44 VH domain

&lt;220&gt;

&lt;223&gt; mouse monoclonal 5/44 VH domain

&lt;220&gt;

&lt;221&gt;

&lt;400&gt; 8

Glu Val Gln Leu Gln Gln Ser Gly Thr Val Leu Ala Arg Pro Gly Ala  
 1 5 10 15

Ser Val Lys Met Ser Cys Lys Ala Ser Gly Tyr Arg Phe Thr Asn Tyr  
 20 25 30

Trp Ile His Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile  
 35 40 45

Gly Gly Ile Asn Pro Gly Asn Asn Tyr Thr Thr Tyr Lys Arg Asn Leu  
 50 55 60

Lys Gly Lys Ala Thr Leu Thr Ala Val Thr Ser Ala Ser Thr Ala Tyr  
65 70 75 80

Met Asp Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys  
85 90 95

Thr Arg Glu Gly Tyr Gly Asn Tyr Gly Ala Trp Phe Ala Tyr Trp Gly  
100 105 110

Gln Gly Thr Leu Val Thr Val Ser Ser  
115 120

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<400> 11

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 <223> T57V

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<400> 12  
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<220>  
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<400> 13  
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Gly

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&lt;220&gt;

&lt;223&gt; CDR-H2 (K60R)R H''

&lt;220&gt;

&lt;221&gt;

&lt;400&gt; 15

Gly Ile Asn Pro Gly Asn Asn Tyr Thr Thr Tyr Arg Arg Asn Leu Lys  
 1 5 10 15

Gly

&lt;210&gt; 16

&lt;211&gt; 17

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; CDR-H2 (T57A K60R) H'''

&lt;220&gt;

&lt;221&gt;

&lt;400&gt; 16

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 1 5 10 15

Gly

&lt;210&gt; 17

&lt;211&gt; 70

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;223&gt; DPK9

&lt;220&gt;

&lt;221&gt;

&lt;400&gt; 17

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly  
 1 5 10 15

Asp Arg Val Thr Ile Thr Cys Trp Tyr Gln Gln Lys Pro Gly Lys Ala  
 20 25 30

Pro Lys Leu Leu Ile Tyr Gly Val Pro Ser Arg Phe Ser Gly Ser Gly  
 35 40 45

Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp  
 50 55 60

Phe Ala Thr Tyr Tyr Cys  
65 70

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<212> PRT  
<213> Homo sapiens

<220>  
<223> JK1

<220>  
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<400> 18  
Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg  
1 5 10

<210> 19  
<211> 113  
<212> PRT  
<213> Artificial Sequence

<220>  
<223> gL1

<220>  
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<400> 19  
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1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ser Ser Gln Ser Leu Ala Asn Ser  
20 25 30

Tyr Gly Asn Thr Phe Leu Ser Trp Tyr Leu His Lys Pro Gly Lys Ala  
35 40 45

Pro Gln Leu Leu Ile Tyr Gly Ile Ser Asn Arg Phe Ser Gly Val Pro  
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile  
65 70 75 80

Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Gly  
85 90 95

Thr His Gln Pro Tyr Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys  
100 105 110

Arg

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 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> gL2

<220>  
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 20 25 30  
 Tyr Gly Asn Thr Phe Leu Ser Trp Tyr Leu His Lys Pro Gly Lys Ala  
 35 40 45  
 Pro Gln Leu Leu Ile Tyr Gly Ile Ser Asn Arg Phe Ser Gly Val Pro  
 50 55 60  
 Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile  
 65 70 75 80  
 Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Gly  
 85 90 95  
 Thr His Gln Pro Tyr Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys  
 100 105 110

Arg

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 <212> PRT  
 <213> Homo sapiens

<220>  
 <223> DP7

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<400> 21  
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 Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Trp Val  
 20 25 30  
 Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met Gly Lys Phe Gln Gly  
 35 40 45



Arg Val Thr Met Thr Arg Asp Thr Ser Thr Ser Thr Val Tyr Met Glu  
 50 55 60

Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg  
 65 70 75 80

<210> 22  
 <211> 11  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <223> JH4

<220>  
 <221>

<400> 22  
 Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser  
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<210> 23  
 <211> 121  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> gH1

<220>  
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<400> 23  
 Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala  
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Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Arg Phe Thr Asn Tyr  
 20 25 30

Trp Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile  
 35 40 45

Gly Gly Ile Asn Pro Gly Asn Gln Tyr Thr Thr Tyr Lys Arg Asn Leu  
 50 55 60

Lys Gly Arg Ala Thr Leu Thr Ala Asp Thr Ser Thr Ser Thr Val Tyr  
 65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys  
 85 90 95

Thr Arg Glu Gly Tyr Gly Asn Tyr Gly Ala Trp Phe Ala Tyr Trp Gly  
 100 105 110

Gln Gly Thr Leu Val Thr Val Ser Ser  
 115 120

<210> 24  
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 <212> PRT  
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<220>  
 <223> gH4

<220>  
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<400> 24  
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 1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Arg Phe Thr Asn Tyr  
 20 25 30

Trp Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile  
 35 40 45

Gly Gly Ile Asn Pro Gly Asn Asn Tyr Ala Thr Tyr Arg Arg Asn Leu  
 50 55 60

Lys Gly Arg Ala Thr Leu Thr Ala Asp Thr Ser Thr Ser Thr Val Tyr  
 65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys  
 85 90 95

Thr Arg Glu Gly Tyr Gly Asn Tyr Gly Ala Trp Phe Ala Tyr Trp Gly  
 100 105 110

Gln Gly Thr Leu Val Thr Val Ser Ser  
 115 120

<210> 25  
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 <212> PRT  
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<220>  
 <223> gH5

<220>  
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<400> 25  
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Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Arg Phe Thr Asn Tyr  
20 25 30

Trp Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile  
35 40 45

Gly Gly Ile Asn Pro Gly Asn Asn Tyr Ala Thr Tyr Arg Arg Asn Leu  
50 55 60

Lys Gly Arg Val Thr Met Thr Ala Asp Thr Ser Thr Ser Thr Val Tyr  
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys  
85 90 95

Thr Arg Glu Gly Tyr Gly Asn Tyr Gly Ala Trp Phe Ala Tyr Trp Gly  
100 105 110

Gln Gly Thr Leu Val Thr Val Ser Ser  
115 120

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<223> gH6

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<400> 26  
Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala  
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Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Arg Phe Thr Asn Tyr  
20 25 30

Trp Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile  
35 40 45

Gly Gly Ile Asn Pro Gly Asn Asn Tyr Ala Thr Tyr Arg Arg Lys Phe  
50 55 60

Gln Gly Arg Ala Thr Leu Thr Ala Asp Thr Ser Thr Ser Thr Val Tyr  
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys  
85 90 95

Thr Arg Glu Gly Tyr Gly Asn Tyr Gly Ala Trp Phe Ala Tyr Trp Gly  
100 105 110

Gln Gly Thr Leu Val Thr Val Ser Ser

115 120

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 <212> PRT  
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<220>  
 <223> gH7

<220>  
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<400> 27  
 Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala  
 1 5 10 15  
 Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Arg Phe Thr Asn Tyr  
 20 25 30  
 Trp Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile  
 35 40 45  
 Gly Gly Ile Asn Pro Gly Asn Asn Tyr Ala Thr Tyr Arg Arg Lys Phe  
 50 55 60  
 Gln Gly Arg Val Thr Met Thr Ala Asp Thr Ser Thr Ser Thr Val Tyr  
 65 70 75 80  
 Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys  
 85 90 95  
 Thr Arg Glu Gly Tyr Gly Asn Tyr Gly Ala Trp Phe Ala Tyr Trp Gly  
 100 105 110  
 Gln Gly Thr Leu Val Thr Val Ser Ser  
 115 120

<210> 28  
 <211> 239  
 <212> PRT  
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<220>  
 <223> Full sequence of grafted light chain

<220>  
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<400> 28  
 Met Lys Leu Pro Val Arg Leu Leu Val Leu Leu Leu Phe Trp Ile Pro  
 1 5 10 15  
 Ala Ser Arg Gly Asp Val Gln Val Thr Gln Ser Pro Ser Ser Leu Ser  
 20 25 30

Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ser Ser Gln Ser  
 35 40 45  
 Leu Ala Asn Ser Tyr Gly Asn Thr Phe Leu Ser Trp Tyr Leu His Lys  
 50 55 60  
 Pro Gly Lys Ala Pro Gln Leu Leu Ile Tyr Gly Ile Ser Asn Arg Phe  
 65 70 75 80  
 Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe  
 85 90 95  
 Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr  
 100 105 110  
 Cys Leu Gln Gly Thr His Gln Pro Tyr Thr Phe Gly Gln Gly Thr Lys  
 115 120 125  
 Val Glu Ile Lys Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro  
 130 135 140  
 Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu  
 145 150 155 160  
 Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp  
 165 170 175  
 Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp  
 180 185 190  
 Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys  
 195 200 205  
 Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln  
 210 215 220  
 Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys  
 225 230 235

<210> 29  
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 <212> DNA  
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 <223> Full sequence of grafted light chain

<220>  
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 ggagaccggg tcaccatcac ttgtagatcc agtcagagtc ttgcaaacag ttatgggaac 180

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ttcacctca cgatctcgtc tctccagcca gaagatttcg ccacttatta ctgtttacaa 360
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gcgcccccat ctgtcttcat cttcccgcc tctgatgagc agttgaaatc tggaactgcc 480
tctgttggtg gcctgctgaa taacttctat cccagagagg ccaaagtaca gtggaagggtg 540
gataacgccc tccaatcggg taactcccag gagagtgtca cagagcagga cagcaaggac 600
agcacctaca gcctcagcag caccctgacg ctgagcaaag cagactacga gaaacacaaa 660
gtctacgcct gcgaagtcac ccatcagggc ctgagctcgc ccgtcacaaa gagcttcaac 720
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<210> 30
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<213> Artificial Sequence

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<220>
<223> Full sequence of grafted heavy chain

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<220>
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Met Asp Phe Gly Phe Ser Leu Val Phe Leu Ala Leu Ile Leu Lys Gly
1 5 10 15
Val Gln Cys Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys
20 25 30
Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Arg Phe
35 40 45
Thr Asn Tyr Trp Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu
50 55 60
Glu Trp Ile Gly Gly Ile Asn Pro Gly Asn Asn Tyr Ala Thr Tyr Arg
65 70 75 80
Arg Lys Phe Gln Gly Arg Val Thr Met Thr Ala Asp Thr Ser Thr Ser
85 90 95
Thr Val Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val
100 105 110
Tyr Tyr Cys Thr Arg Glu Gly Tyr Gly Asn Tyr Gly Ala Trp Phe Ala
115 120 125
Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys
130 135 140
Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu
145 150 155 160
Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro

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| 165 |     |     |     |     | 170 |     |     |     |     | 175 |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Val | Thr | Val | Ser | Trp | Asn | Ser | Gly | Ala | Leu | Thr | Ser | Gly | Val | His | Thr |
|     |     |     | 180 |     |     |     |     | 185 |     |     |     |     | 190 |     |     |
| Phe | Pro | Ala | Val | Leu | Gln | Ser | Ser | Gly | Leu | Tyr | Ser | Leu | Ser | Ser | Val |
|     |     | 195 |     |     |     |     | 200 |     |     |     |     | 205 |     |     |     |
| Val | Thr | Val | Pro | Ser | Ser | Ser | Leu | Gly | Thr | Lys | Thr | Tyr | Thr | Cys | Asn |
|     | 210 |     |     |     |     | 215 |     |     |     |     | 220 |     |     |     |     |
| Val | Asp | His | Lys | Pro | Ser | Asn | Thr | Lys | Val | Asp | Lys | Arg | Val | Glu | Ser |
| 225 |     |     |     |     |     | 230 |     |     |     |     | 235 |     |     |     | 240 |
| Lys | Tyr | Gly | Pro | Pro | Cys | Pro | Pro | Cys | Pro | Ala | Pro | Glu | Phe | Leu | Gly |
|     |     |     |     | 245 |     |     |     |     | 250 |     |     |     |     | 255 |     |
| Gly | Pro | Ser | Val | Phe | Leu | Phe | Pro | Pro | Lys | Pro | Lys | Asp | Thr | Leu | Met |
|     |     |     | 260 |     |     |     |     | 265 |     |     |     |     | 270 |     |     |
| Ile | Ser | Arg | Thr | Pro | Glu | Val | Thr | Cys | Val | Val | Val | Val | Asp | Val | Ser |
|     |     | 275 |     |     |     |     | 280 |     |     |     |     |     | 285 |     | Gln |
| Glu | Asp | Pro | Glu | Val | Gln | Phe | Asn | Trp | Tyr | Val | Asp | Gly | Val | Glu | Val |
|     | 290 |     |     |     |     | 295 |     |     |     |     | 300 |     |     |     |     |
| His | Asn | Ala | Lys | Thr | Lys | Pro | Arg | Glu | Glu | Gln | Phe | Asn | Ser | Thr | Tyr |
| 305 |     |     |     |     |     | 310 |     |     |     |     | 315 |     |     |     | 320 |
| Arg | Val | Val | Ser | Val | Leu | Thr | Val | Leu | His | Gln | Asp | Trp | Leu | Asn | Gly |
|     |     |     |     | 325 |     |     |     |     | 330 |     |     |     |     | 335 |     |
| Lys | Glu | Tyr | Lys | Cys | Lys | Val | Ser | Asn | Lys | Gly | Leu | Pro | Ser | Ser | Ile |
|     |     |     | 340 |     |     |     |     | 345 |     |     |     |     | 350 |     |     |
| Glu | Lys | Thr | Ile | Ser | Lys | Ala | Lys | Gly | Gln | Pro | Arg | Glu | Pro | Gln | Val |
|     |     | 355 |     |     |     |     | 360 |     |     |     |     | 365 |     |     |     |
| Tyr | Thr | Leu | Pro | Pro | Ser | Gln | Glu | Glu | Met | Thr | Lys | Asn | Gln | Val | Ser |
|     | 370 |     |     |     |     | 375 |     |     |     |     | 380 |     |     |     |     |
| Leu | Thr | Cys | Leu | Val | Lys | Gly | Phe | Tyr | Pro | Ser | Asp | Ile | Ala | Val | Glu |
| 385 |     |     |     |     |     | 390 |     |     |     |     | 395 |     |     |     | 400 |
| Trp | Glu | Ser | Asn | Gly | Gln | Pro | Glu | Asn | Asn | Tyr | Lys | Thr | Thr | Pro | Pro |
|     |     |     |     | 405 |     |     |     |     | 410 |     |     |     |     | 415 |     |
| Val | Leu | Asp | Ser | Asp | Gly | Ser | Phe | Phe | Leu | Tyr | Ser | Arg | Leu | Thr | Val |
|     |     |     | 420 |     |     |     |     | 425 |     |     |     |     | 430 |     |     |
| Asp | Lys | Ser | Arg | Trp | Gln | Glu | Gly | Asn | Val | Phe | Ser | Cys | Ser | Val | Met |
|     |     | 435 |     |     |     |     | 440 |     |     |     |     | 445 |     |     |     |
| His | Glu | Ala | Leu | His | Asn | His | Tyr | Thr | Gln | Lys | Ser | Leu | Ser | Leu | Ser |
|     | 450 |     |     |     |     | 455 |     |     |     |     | 460 |     |     |     |     |

Leu Gly Lys  
465

<210> 31  
<211> 2160  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Full DNA sequence of grafted heavy chain

<220>  
<221>

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&lt;400&gt; 40

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87

&lt;210&gt; 41

&lt;211&gt; 90

&lt;212&gt; DNA

&lt;213&gt; Artificial Sequence

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90

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&lt;212&gt; DNA

&lt;213&gt; Artificial Sequence

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&lt;223&gt; 544gL1 T3

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&lt;400&gt; 42

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&lt;212&gt; DNA

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&lt;223&gt; 544gL1 B2

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<400> 55

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Thr Met Thr Ala  
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<400> 61

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| Ser | Arg | Gly | Asp | Val | Val | Val | Thr | Gln | Ser | Pro | Ser | Ser | Leu | Ser | Ala |
| 1   |     |     |     | 5   |     |     |     | 10  |     |     |     |     | 15  |     |     |

|     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|
| Ser | Val | Gly | Asp | Arg | Val | Thr |
|     |     |     | 20  |     |     |     |